



Bureau International des Poids et Mesures

JCTLM Meeting 2008



Joint Committee for Traceability in Laboratory Medicine

**A Database of Higher Order Reference Materials
and Reference Measurement Procedures**

R.I. Wielgosz, BIPM

www.bipm.org

Joint Committee for **Traceability** in Laboratory Medicine

- What has it done?
- Why is it important?
- How does it carry out its tasks?
- What does the database look like?
- How can the database be used?
- What are the JCTLM's future activities?



What has JCTLM delivered?

A Quality assured database of:

- a) Higher Order Reference Materials**
- b) Reference Measurement Procedures**
- c) Laboratory Reference Measurement Services (2007)**

<http://www.bipm.org/jctlm/>

For use by (primarily)

- a) IVD industry**
- b) Regulators**



The IVD Directive of the EU requires that:

"The traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order.. "

**Annex I - Essential Requirements
Part A. General Requirements, Clause 3**



Aim of the IVD Directive

“to ensure that IVDs do not compromise the health and safety of patients, users and third parties and attain the performance levels attributed to them by their manufacturer. ”

MHRA, UK Guidance 2006



Why is Traceability an essential requirement?

Non-traceable IVD measurement systems can lead to:

- Lack of product control***
- Non comparable measurement results***
- Incorrect patient diagnosis and treatment***
- Uncertainty of compliance with the Directive***

What Is Metrological Traceability?

- Definition VIM, 3rd edition, JCGM 200:2008

Metrological traceability - property of a measurement result whereby the result can be related to **a reference** through a documented unbroken chain of **calibrations**, each contributing to the **measurement uncertainty**

Measurement Uncertainty Definition

VIM III, 2.26

- **measurement uncertainty** –
non-negative parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used

Glucose in Blood, Serum, Urine, CSF
SI-Unit: mmol/l

*Definition
of the measurand*

Section 1 –External to manufacturer, credentialing of the Certified Reference Material

SRM917b

NIST certification of SRM917b (purity)

Primary calibrator

SRM917b – weighed amount

Weighing procedure

Primary reference measurement procedure

Secondary calibrator

Human Patient Specimens, e.g. Blood, Serum, Urine, CSF

Higher Order Reference Procedure – e.g. Isotope Dilution - Mass Spectrometry or Procedure of Similar Trueness and Precision

Secondary reference measurement procedure

Section 2 –Internal to manufacturer, value assignment

Manufacturer's working calibrator

Manufacturer's Master Calibrator, Master Lot of Product Calibrator

Reference Procedure traceable to higher order reference procedure - e.g. Hexokinase/glucose-6-phosphate Dehydrogenase Procedure

Manufacturer's selected measurement procedure

Product Calibrator

New Lot Commercial Product Calibrator

Procedure applying same chemistry and equipment as routine procedure, but more precisely controlled conditions and more replicates to reduce uncertainty

Manufacturer's standing measurement procedure

Section 3 –External to manufacturer, End user's results are Traceable to Certified Reference Material and the Reference System

Commercially available system including product reagent and calibrator lots

End user's routine measurement procedure

Routine Sample – Human Patient Specimens, e.g. Blood, Serum, Urine or CSF

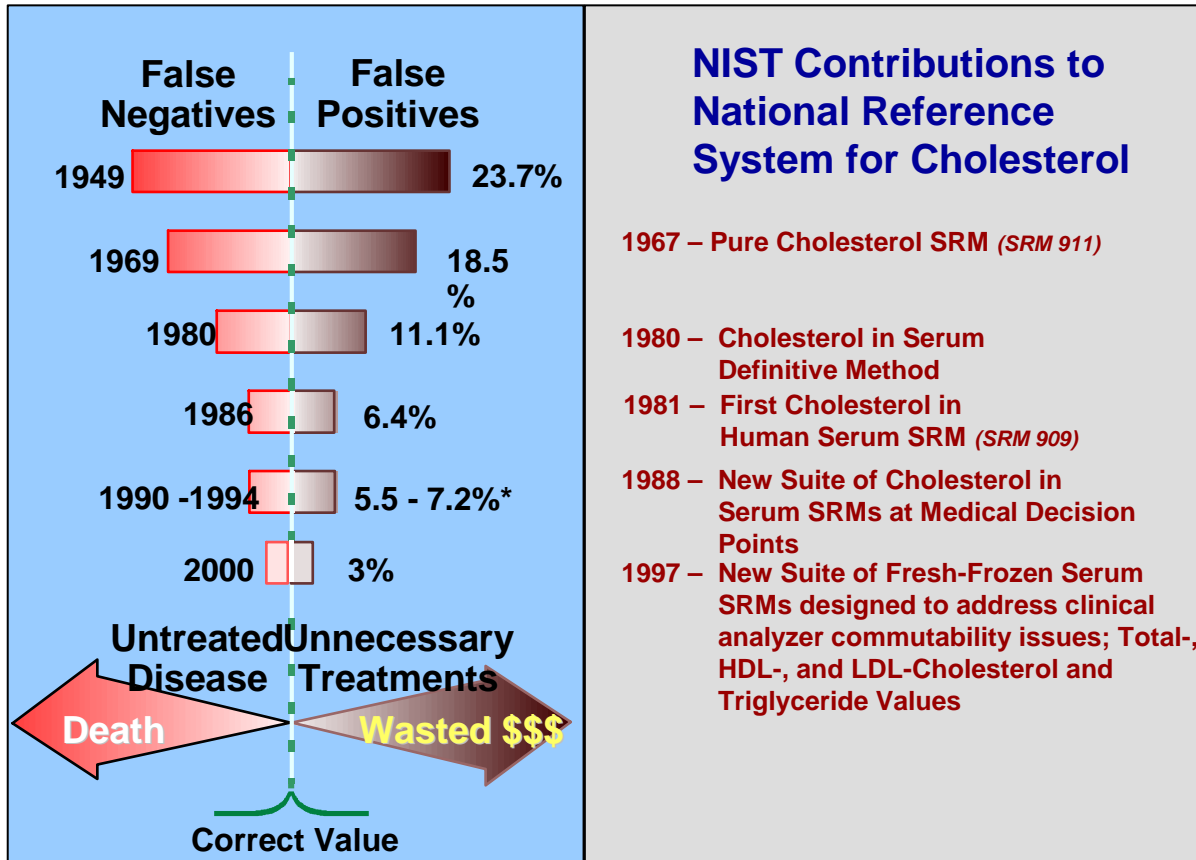
RESULT
Glucose in mmol/l

Traceability Chain for the Measurement of Glucose in Body Fluids

Why Traceability

- Evidence Based Medicine is becoming more and more prominent in the practice of clinical laboratory science
 - Glucose
 - PSA
 - HbA1c
 - Creatinine (GFR calculations)
- All of these analytes have specific cutoffs that are independent of the assay used.
- To correctly utilize these cutoffs, the assays for the analyte in question must be comparable.

Improved Cholesterol Measurement Accuracy Reduces Health Care Costs and Improves Patient Care



Improvement in precision since 1968 has been estimated to save \$100M/yr in treatment costs

Data from U.S. Government Accounting Office and College of American Pathologists



Sponsoring Organizations



**Intergovernmental Treaty Organization
for Measurement Standards**



**International NGO for Professionals in
Laboratory Medicine**



**International NGO for Accreditation
Bodies**

DECLARATION OF COOPERATION

The **International Committee of Weights and Measures (CIPM)**, the **International Federation for Clinical Chemistry and Laboratory Medicine (IFCC)**, and the **International Laboratory Accreditation Cooperation (ILAC)** have agreed to cooperate to establish a Joint Committee for Traceability in Laboratory Medicine, with the acronym **JCTLM**.

The goal of the JCTLM is to provide a worldwide platform to promote and give guidance on internationally recognized and accepted equivalence of measurements in laboratory medicine and traceability to appropriate measurement standards.

Chair

IFCC:



Prof Jean Claude Forest

Centre Hospitalier Universitaire de Québec
et Université Laval
Québec
Canada

Secretariat

BIPM:



Dr Robert Wielgosz

Bureau International des Poids et Mesures
Pavillon de Breteuil
F-92312 SÈVRES CEDEX
France



Operational Structure

- **Executive Committee**
- **Working Groups**
 1. **Reference Materials and Reference Methods**

Chairs: W. May (NIST), H. Schimmel (IRMM),
Compilation of existing RMPs and CRMs (Lists)
 2. **Reference Laboratories - Networks**

Chairs: L. Siekmann, L. Thienpont (IFCC)
Lists of Laboratory Reference Measurement
Services (RMSs)
Guidelines for reference laboratories

Relevant ISO Standards for higher order RMs and RMPs

ISO 17511 In vitro diagnostic medical devices - Measurement of quantities in biological samples - Metrological traceability of values assigned to calibrators and control materials

ISO 18153 Metrological traceability of values for catalytic concentration of enzymes assigned to calibrators and control materials

ISO 15193 Presentation of reference measurement procedures

ISO 15194 Description of reference materials

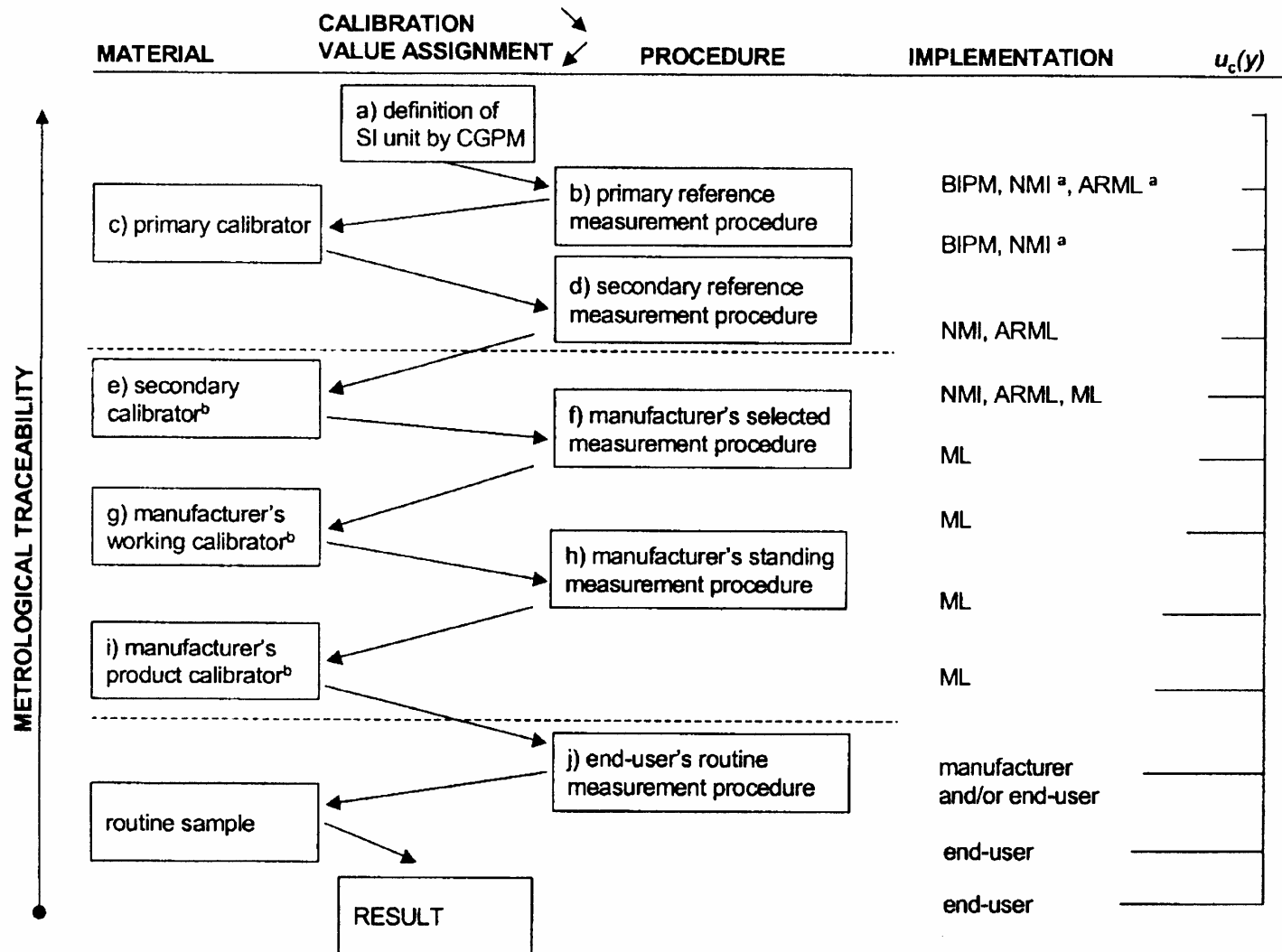
ISO 15195 Reference Measurement Laboratories

JCTLM-WG1 Quality Manual:
Reference Materials and Reference Procedures

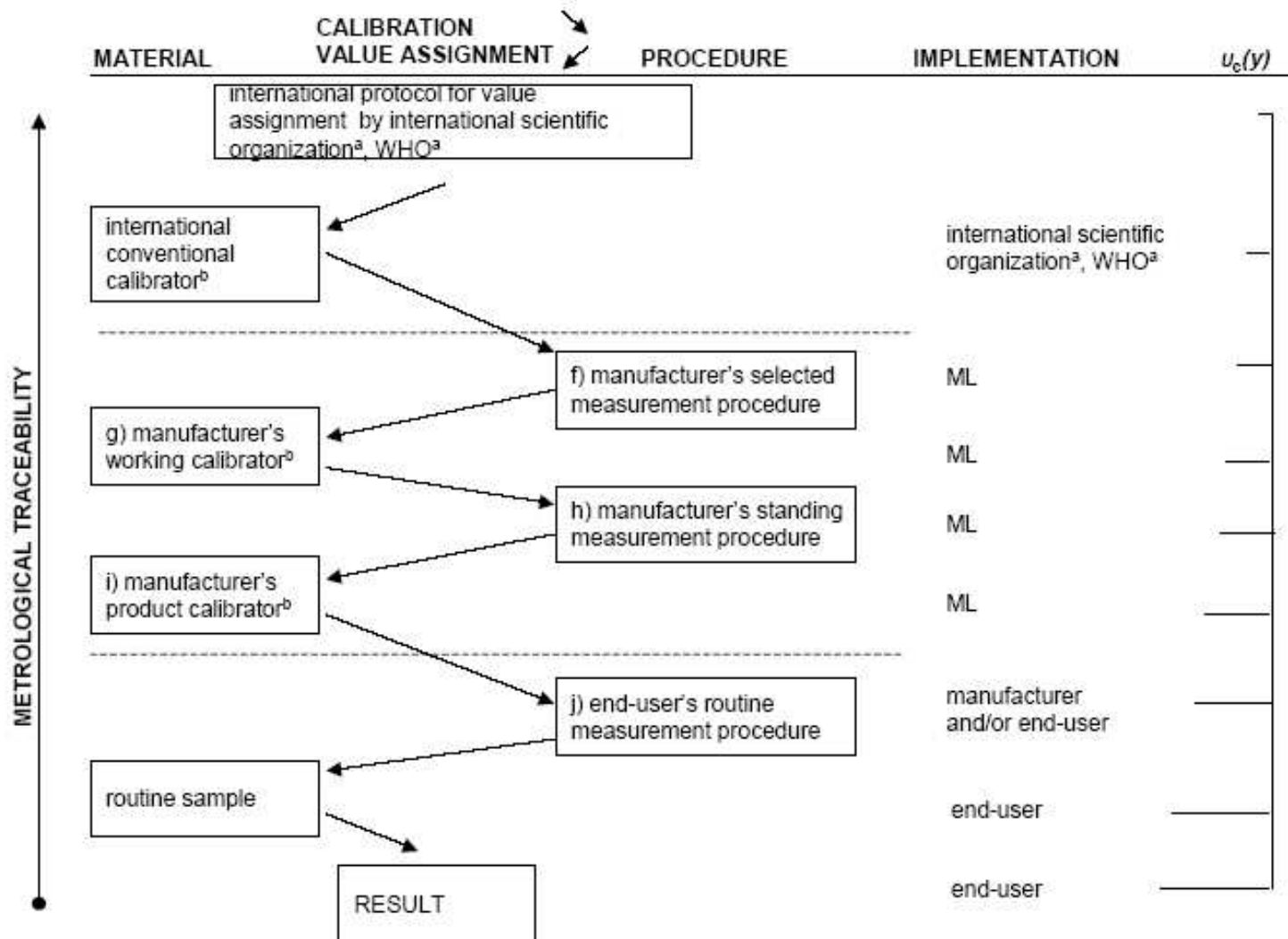


✓	<u>Preamble</u>		PDF	2006/01/31
✓	<u>WG1-P-00</u>	Quality Policy	PDF	2006/01/30
✓	<u>WG1-P-01</u>	Outline of JCTLM procedures	PDF	2006/01/31
✓	<u>WG1-P-02</u>	Reference material and procedure nomination requests	PDF	2006/01/31
✓	<u>WG1-P-02-F-01 & F-02</u>	Reference material and procedure nomination templates	✗	2006/01/30
✓	<u>WG1-P-02-F-01 EXAMPLE</u>	Reference material nomination example	✗	2006/01/30
✓	<u>WG1-P-02-F-02 EXAMPLE</u>	Reference procedure nomination example	✗	2006/01/30
✓	<u>WG1-P-02-I-01</u>	Instructions for completing nomination templates	PDF	2006/01/31
✓	<u>WG1-P-03</u>	Review and approval of nominations	PDF	2006/01/30
✓	<u>WG1-P-03-F-03</u>	Review report form	DOC	2006/01/30
✓	<u>WG1-P-04A</u>	Multiple CRM comparison process	PDF	2006/01/30
✓	<u>WG1-P-04B</u>	Multiple reference method/procedure comparison process	PDF	2006/01/30
✓	<u>WG1-P-05</u>	Consensus review and communication of recommendations	PDF	2006/01/30
✓	<u>WG1-P-06</u>	Membership of JCTLM WG1 Review Teams	PDF	2006/01/31
✓	<u>WG1-P-06-F-01</u>	Review Team membership form	DOC	2006/01/30
✓	<u>WG1-P-07</u>	Process for changing the WG1 Quality System procedures	PDF	2006/01/31
✓	<u>WG1-P-07-F-01</u>	Procedure change request form	DOC	2006/01/30
✓	<u>WG1-P-08</u>	Process for changing WG Review Teams	PDF	2006/01/30
✓	<u>WG1-P-09</u>	Appeals process	PDF	2006/01/30

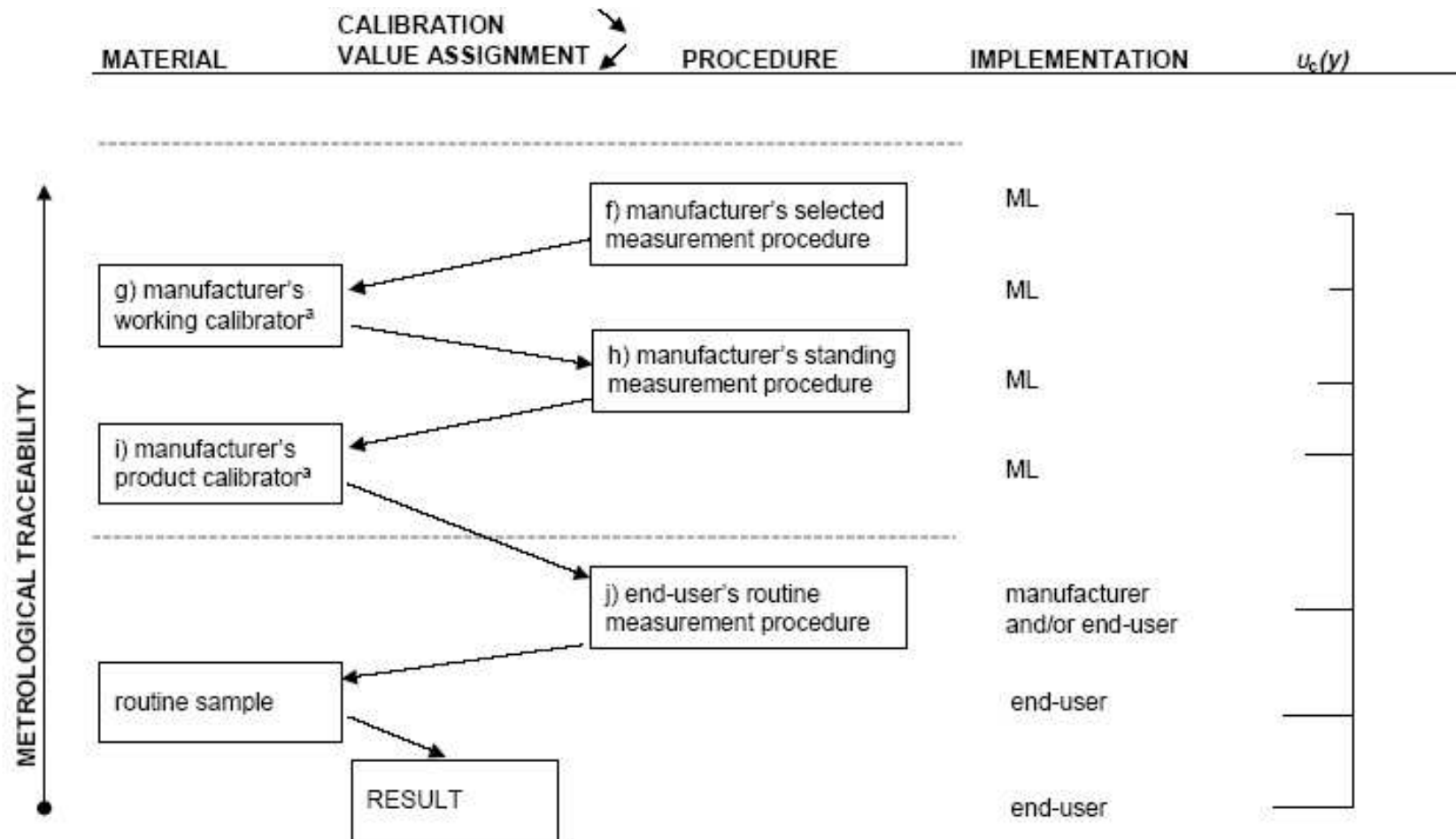
SI traceability - Primary Calibrators (ISO 17511)



Traceability to an international conventional calibrator (ISO 17511)



Traceability to manufacturer's selected measurement procedure (ISO 17511)



JCTLM WG1 Review Process

INTERNATIONAL
STANDARD

ISO
15194

First edition
2002-10-01

***In vitro* diagnostic medical devices —
Measurement of quantities in samples of
biological origin — Description of reference
materials**

*Dispositifs médicaux de diagnostic in vitro — Mesure des grandeurs dans
les échantillons d'origine biologique — Description des matériaux de
référence*



Reference number
ISO 15194:2002(E)

© ISO 2002

JCTLM WG1 Review Process (ISO 15194)

5 Description of a reference material

5.1 Elements of a description

The description of a reference material of higher metrological order shall comprise at least the elements listed as mandatory (M) in Table 1.

NOTE: The order of the elements listed in Table 1 may be changed and additional elements, such as an abstract, may be added as appropriate.

Table 1: Main elements (clauses) of a report describing a reference material of higher metrological order

Element	Type ¹⁾		Subclause in this European Standard
	M	O	
Title page	I		
Contents list		I	
Foreword	I		
Warning and safety precautions	N		5.2
Introduction		I	5.3
Title of report	N		
Scope	N		5.4
Definitions		N	
Symbols and abbreviations		N	
Terminology		N	5.5
Justification for choice of reference material	I		5.6
General characteristics	I		5.7
Specific characteristics	I		5.8
Validation	I		5.9
Intended function	I		5.10
Instructions for use	I		5.11
Supplier	I		5.12
Bibliography		I	5.13
Annexes		I	5.14
Dates	I		5.15
¹⁾ Symbols for type of element in a European Standard: M mandatory, O optional; I informative, N normative.			

Summary of Cycles I & II Nominations and Approvals

Category	Number of Nominations Submitted		Number Recommended for Publication	
	Reference Materials	Reference Measurement Procedures	Reference Materials	Reference Measurement Procedures
Blood Gases	1	1	0	0
Drugs	84	5	23	3
Electrolytes	70	23	29	23
Enzymes	20	7	11	6
Metabolites and Substrates	69	44	39	35
Non-Electrolyte Metals	43	50	30	15
Non-Peptide Hormones	15	26	14	22
Nucleic Acids	5	0	0	0
Vitamins	8	2	7	0
Proteins	114	20	43	19
Blood Groupings	3	0	0	0
Coagulation Factor	34	0	12	0
Microbial Serology	10	8	0	0
Other	6	2	3	0
TOTAL Number	482	188	211	123

LIST I

published initially on 01 April 2004

Certified Reference Materials and Reference Measurement Procedures for well-defined chemical entities or internationally recognized reference method-defined measurands, such as enzymes. Reference Materials included in this category are those that are traceable to the SI units. [*Electrolytes, Drugs, Metabolites and Substrates, Non-Peptide Hormones, Enzymes and some Proteins*]

approximately **123** Reference Measurement Procedure entries for **75** different health status markers

approximately **211** Reference Material entries for **128** measurands

<http://www.bipm.org/en/committees/jc/jctlm/jctlm-db/>

JCTLM LIST II

Reference Materials that are value-assigned using an internationally agreed upon protocol e.g., reference materials for Blood Typing, Coagulation Factors, Microbial Serology, Nucleic Acids, and some Proteins. The values of the measurands in the reference materials on this List are not SI-traceable and/or no internationally-recognized reference measurement procedures exist.

Initially published in January, 2005, now includes

- 21 CRMs for Coagulation Factors
- 7 CRMs for Proteins
- 3 CRMs for Blood Groupings
- 2 CRMs for Enzymes

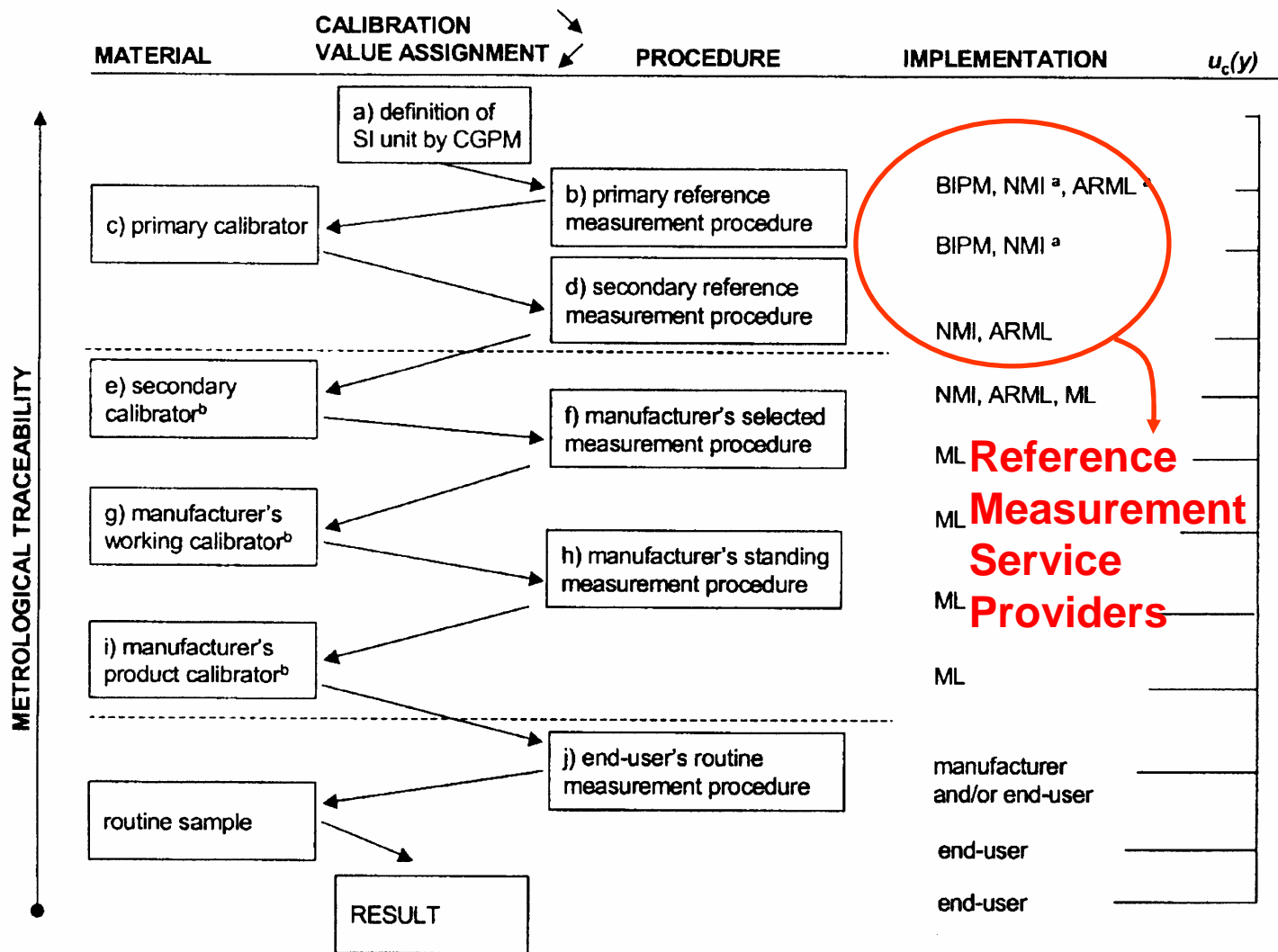
Reference Measurement Laboratories

JCTLM Working Group II - Reference Measurement Services

Assessed on basis of:

- **Metrological level of the reference procedures used (compliance with JCTLM WG1 RMPs)**
- **Accreditation to ISO 17025 and ISO 15195 as a calibration laboratory and/or CIPM-MRA process**
- **Ongoing performance in inter-laboratory comparisons**

SI traceability - Primary Calibrators (ISO 17511)



JCTLM Working Group II - Reference Measurement Services for Laboratory Medicine

JCTLM-WG2 Procedure Manual:
Reference Measurement Services



		Title	File type	Last update
↓	<u>WG2-P-00</u>	Outline of calibration hierarchy in laboratory medicine	PDF	2006/01/30
↓	<u>WG2-P-01</u>	Overview of JCTLM WG2 procedures	PDF	2006/01/30
↓	<u>WG2-P-02</u>	Nomination process for reference measurement laboratory services	PDF	2006/01/31
↓	<u>WG1-P-02-F-01</u>	Template for nomination of reference laboratory measurement services		2006/01/30
↓	<u>WG2-P-03A</u>	Review of NMI measurement services	PDF	2006/01/30
↓	<u>WG2-P-03B</u>	Review of measurement services from accredited laboratories	PDF	2006/01/30
↓	<u>WG2-P-03C</u>	Review of measurement services from laboratories preparing for accreditation	PDF	2006/01/30
↓	<u>WG2-P-04</u>	Listing reference measurement laboratory services	PDF	2006/01/30
↓	<u>WG2-P-05</u>	De-listing reference measurement laboratory services	PDF	2006/01/30



Reference Laboratories in Laboratory Medicine

Registration Form for Ring Trial RELA 01/2004

Reference Laboratory Address:

Organisation:	Laboratory
Name of person responsible:	Name
Street:	
City:	
Post Code:	
State:	
Country:	
Phone:	
Fax:	
e-mail:	

Please return by August 15, 2004 to:

Dr. R. Kruse,
Dr. W. Geilenkeuser
DGKL
Im Mühlenbach 52 a
D-53127 Bonn - Germany

Fax: +49-228-211529
E-mail: info@dgkl-rfb.de

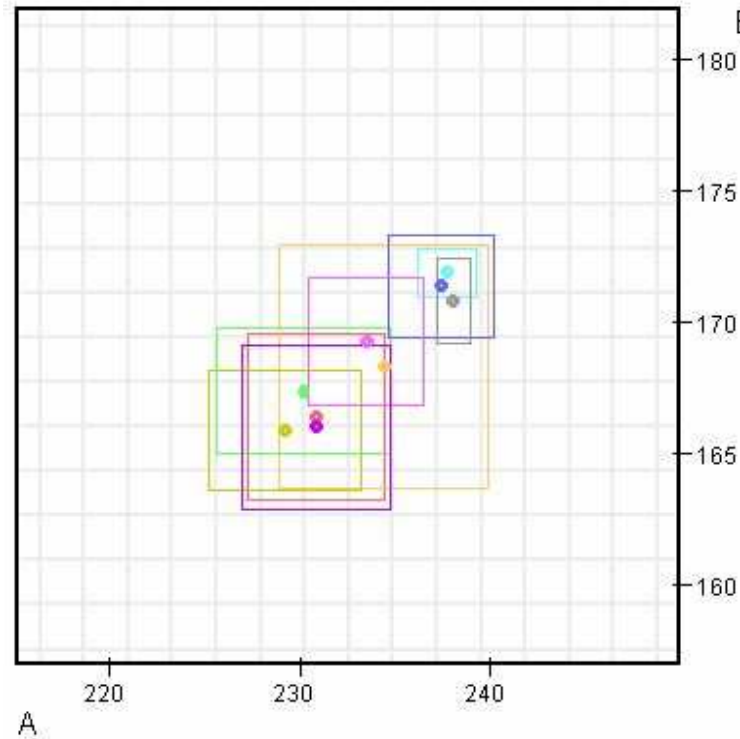
Please switch to next table (Measurands) !

	A	B	C
11			
12	Measurand	Participation please indicate "X"	Number of Vials
13			
14			
15			
16	METABOLITES & SUBSTRATES		
17	Total Cholesterol		
18	Total Glycerol		
19	Creatinine	x	2 x 5
20	Uric Acid		
21	Urea		
22	Glucose		
23	Total Bilirubine		
24			
25	ELECTROLYTES		
26	Sodium		
27	Potassium	x	2 x 5
28	Chloride		
29	Calcium		
30	Lithium		
31	Magnesium		
32			
33	ENZYMES		
34	ALT		
35	AST		
36	CK		
37	LDH		
38	GGT		
39	Amylase		
40			
41	Total Protein		
42			
43	HORMONES		
44	Aldosterone		
45	Cortisol	x	2 x 5
46	Progesterone		
47	Testosterone		
48	Estradiol-17β		
49	Estriol (non-conjugates)		
50	Total Thyroxine (TT4)		
51	Total Tri-iodothyronine (TT3)		
52	17-Hydroxyprogesterone		
53			
54	THERAP.DRUGS		
55	Digoxin	x	2 x 5
56	Digitoxin		
57	Theophyllin		

IFCC EQAS, Inter-laboratory comparisons for Reference Measurement Laboratories

RELA 1/2003

Total cholesterol [mg/dl]



Lab	A	p.e.u.	B	p.e.u.	method
01	230,888	3,572	166,409	3,175	ID-MS
05	234,43	5,523	168,31	4,641	ID-MS
08	229,227	4,028	165,907	2,262	ID-MS
11	230,2	4,613	167,4	2,369	ID-MS
12	237,8	1,558	171,9	0,890	spectrometry (Abell-Kendall)
16	237,490	2,764	171,389	1,962	spectrometry (Abell-Kendall)
18	233,5	3,08	169,3	2,42	HPLC
19	238,1	0,860	170,8	1,610	spectrometry (Abell-Kendall)
27	230,888	3,919	166,023	3,105	ID-MS

<http://www.dgkl-rfb.de:81>

JCTLM Database: Search Engine



Bureau International des Poids et Mesures

Database of higher-order reference materials,
measurement methods/procedures and services



JCTLM Database
Laboratory medicine and *in vitro* diagnostics

> You are here : JCTLM-DB



JCTLM database: Laboratory medicine and *in vitro* diagnostics

↳ JCTLM-DB

- ↳ [Search Form](#)
- ↳ [General information](#)
- ↳ [List of reference materials no longer listed](#)
- ↳ [Leaflet](#)
- ↳ [Contact us](#)

↳ Highlights

- ↳ [Extension of the JCTLM-DB](#)
- ↳ [Publication of new data](#)

↳ JCTLM

- ↳ [General information](#)

↳ Analyte keyword search for reference materials, measurement methods/procedures and services

Type an analyte name in part or full, e.g. cholesterol

Refine search by analyte category

Refine search by matrix category

Please select your requirement :

- Higher-order reference materials
- Reference measurement methods/procedures
- Reference measurement services

Reset ×

Search →

Content of the JCTLM Database (January 2008)

Certified Reference Materials (CRMs) =	202
CRMs no longer listed =	28
Reference Measurement Methods =	139
Laboratory Reference Measurement Services =	98

Download all entries for a specific analyte or matrix category as PDF

Please select your requirement :

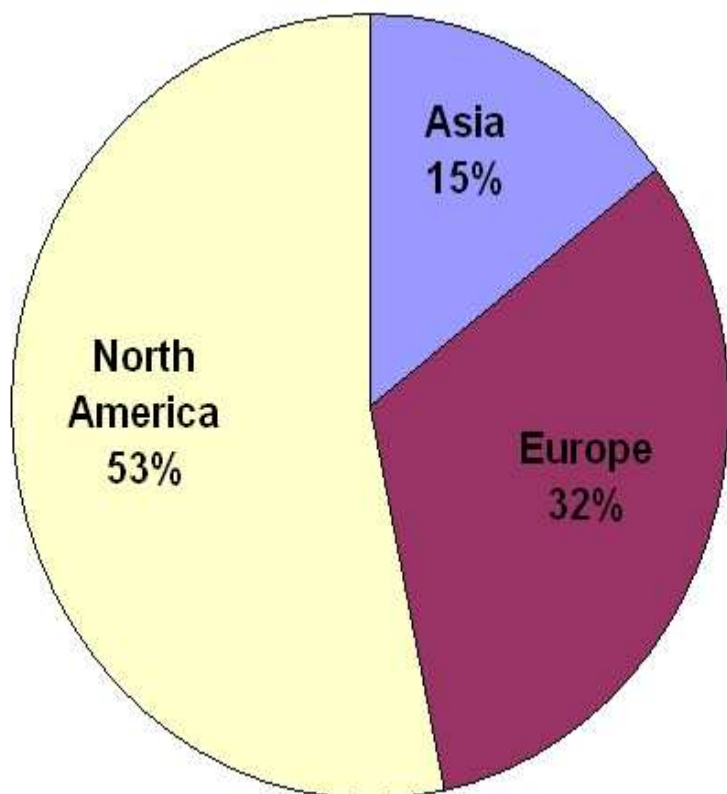
- Higher-order reference materials
- Reference measurement methods/procedures
- Reference measurement services

Select an analyte category

Select a matrix category

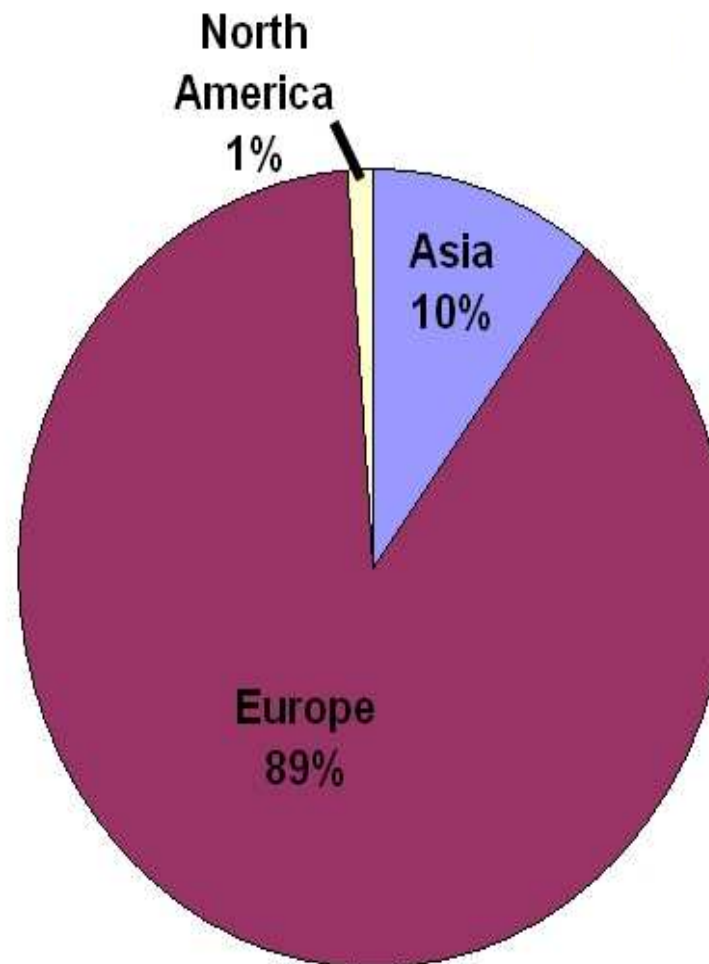
JCTLM Database: Summary of entries by Region of Origin

Certified Reference Materials



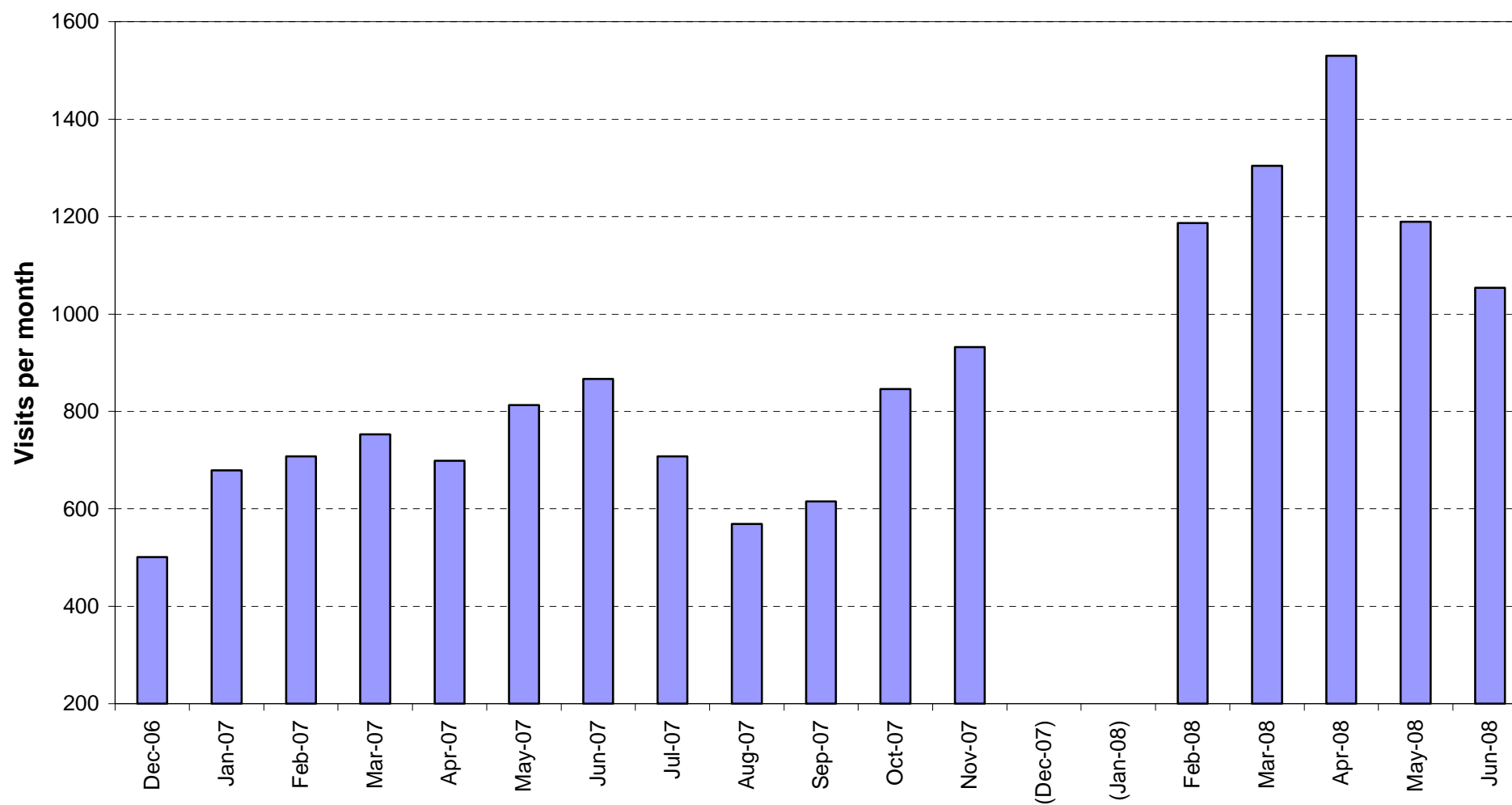
Entries = 202

Reference Measurement Services



Entries = 98

JCTLM Database: Visits per Month



Note: No data available for December 2007 and January 2008

Using the JCTLM Database

Establishing and validating a traceable
measurement system



Glucose in Blood, Serum, Urine, CSF
SI-Unit: mmol/l

**Combined
standard
uncertainty (%)**

Section 1 –External to manufacturer, credentialing of the Certified Reference Material

SRM917b

NIST certification of SRM917b (purity)

0.1%

Primary calibrator

SRM917b – weighed amount

Weighing procedure

0.87%

Secondary calibrator

Human Patient Specimens, e.g. Blood, Serum, Urine, CSF

Higher Order Reference Procedure – e.g. Isotope Dilution - Mass Spectrometry or Procedure of Similar Trueness and Precision

Section 2 –Internal to manufacturer, value assignment

Manufacturer's working calibrator

Manufacturer's Master Calibrator, Master Lot of Product Calibrator

Reference Procedure traceable to higher order reference procedure - e.g. Hexokinase/glucose-6-phosphate Dehydrogenase Procedure

1.21%

Product Calibrator

New Lot Commercial Product Calibrator

Procedure applying same chemistry and equipment as routine procedure, but more precisely controlled conditions and more replicates to reduce uncertainty

1.49%

Section 3 –External to manufacturer, End user's results are Traceable to Certified Reference Material and the Reference System

Commercially available system including product reagent and calibrator lots

Routine Sample – Human Patient Specimens, e.g. Blood, Serum, Urine or CSF

RESULT
Glucose in mmol/l

Glucose in Blood, Serum, Urine, CSF
SI-Unit: mmol/l

**Combined
standard
uncertainty (%)**

Section 1 –External to
manufacturer, credentialing of the
Certified Reference Material

JCTLM ACTIVITIES

ISO 15193, ISO 15194, ISO 15195

Characterization of SRM917b

0.1%

Weighing procedure

Higher Order Reference Procedure –
e.g. Isotope Dilution - Mass
Spectrometry or Procedure of Similar
Trueness and Precision

0.87%

Secondary calibrator

Human Patient Specimens,
e.g. Blood, Serum, Urine,
CSF

Section 2 –Internal to
manufacturer, value assignment

Reference Procedure traceable to
higher order reference procedure -
e.g. Hexokinase/glucose-6-

1.21%

*Manufacturer's
working calibrator*

Manufacturer's Master
Calibrator, Master Lot of
Product Calibrator

phosphate Dehydrogenase
Procedure

Procedure applying same chemistry
and equipment as routine procedure,
but more precisely controlled
conditions and more replicates to
reduce uncertainty

1.49%

Product Calibrator

New Lot Commercial
Product Calibrator

Section 3 –External to
manufacturer, End user's results are
Traceable to Certified Reference Material
and the Reference System

Commercially available system
including product reagent and
calibrator lots

Routine Sample – Human Patient Specimens,
e.g. Blood, Serum, Urine or CSF

ISO 15189

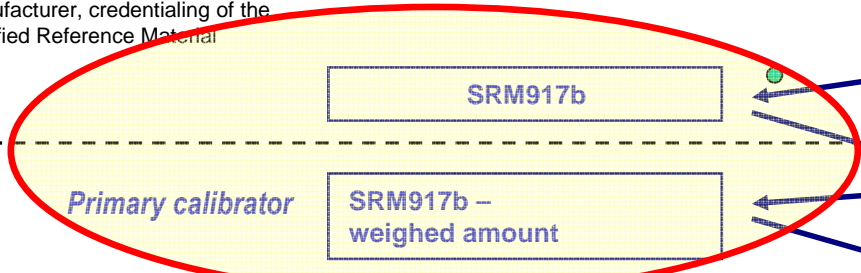
RESULT
Glucose in mmol/l

ISO 17511

Glucose in Blood, Serum, Urine, CSF
SI-Unit: mmol/l

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Routine Sample – Human Patient Specimens, e.g. Blood, Serum, Urine or CSF

RESULT
Glucose in mmol/l

JCTLM Database: Glucose Certified Reference Materials

Results of the search

glucose in glucose crystalline material

National Institute of Standards and Technology (NIST), United States

Phone: +1 301 975 6776

Email: srminfo@nist.gov

Fax: +1 301 948 3730

Web: <http://www.nist.gov/srm>

Name of the reference material	SRM 917b, D-glucose (dextrose)
Quantity	Mass fraction
Analyte certified/assigned value	99.7 %
Expanded uncertainty (level of confidence 95%)	0.2 %
Reference(s) on commutability	Not applicable: a high-purity material used as a primary calibrator for higher order reference methods
Traceability	SI
CRM listing	List I

glucose in human serum

National Institute of Standards and Technology (NIST), United States

Phone: +1 301 975 6776

Email: srminfo@nist.gov

Fax: +1 301 948 3730

Web: <http://www.nist.gov/srm>

Name of the reference material	SRM 965a, glucose in frozen human serum
Quantity	Amount-of-substance concentration
Analyte certified/assigned value	1.918 mmol/l to 16.24 mmol/l
Expanded uncertainty (level of confidence 95%)	0.02 mmol/l to 0.19 mmol/l
Other relevant publication(s)	Method used for certification: <i>Biomed. Mass Spectrom.</i> , 1982, 9 , 395-405
Traceability	SI
CRM listing	List I

Glucose in Blood, Serum, Urine, CSF
SI-Unit: mmol/l

**Combined
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Commercially available system including product reagent and calibrator lots

Routine Sample – Human Patient Specimens, e.g. Blood, Serum, Urine or CSF

RESULT
Glucose in mmol/l

JCTLM Database: Reference Methods for Glucose

Results of the search

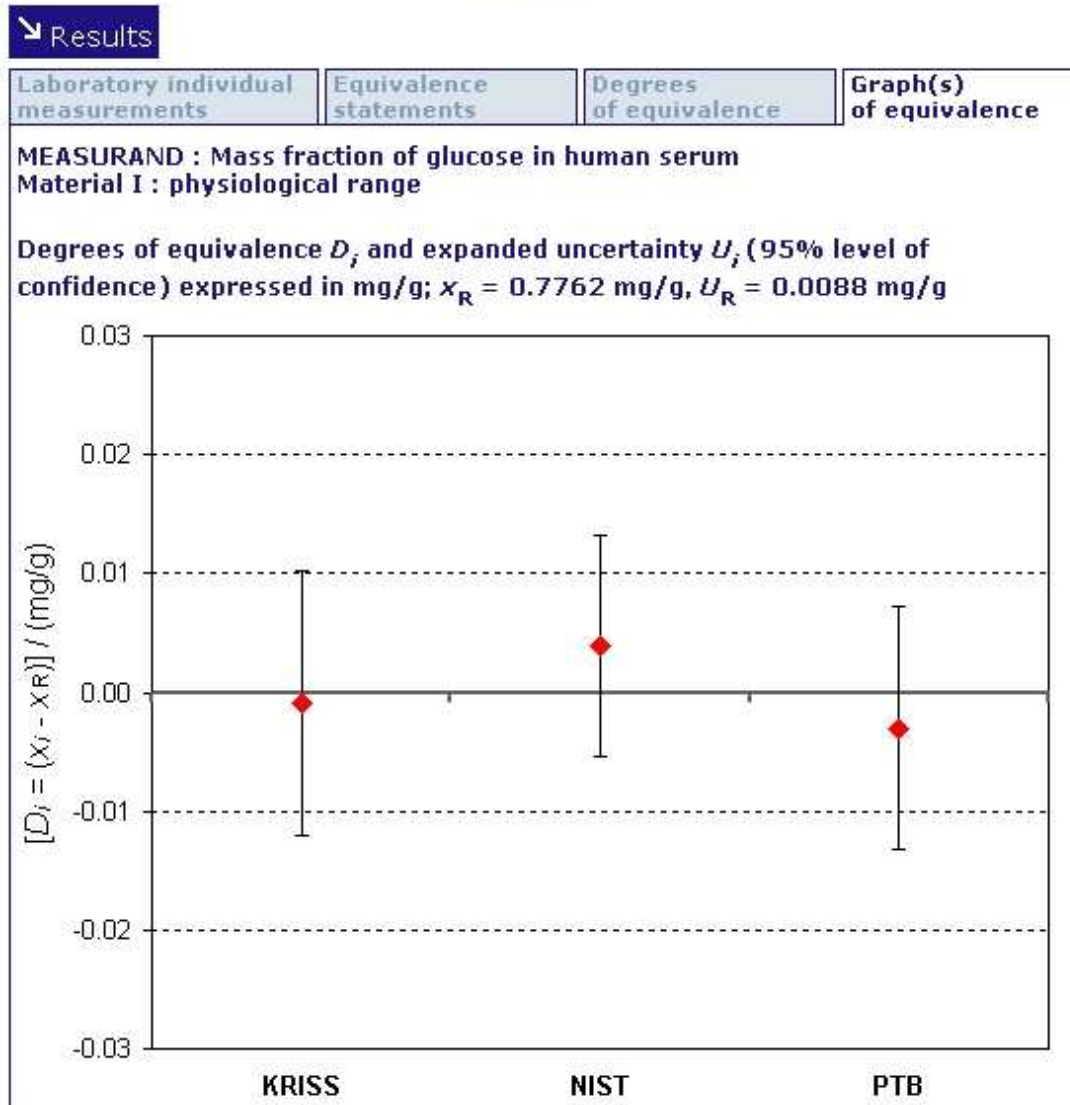
Isotope dilution mass spectrometry methods for glucose in blood serum	
▸ NIST definitive method for serum glucose	
Applicable matrice(s)	lyophilized, fresh, or frozen human serum
Full description of technique(s)	ID/GC/MS
Quantity	Amount-of-substance concentration
Applicable range	2 mmol/l to 20 mmol/l
Expected uncertainty (level of confidence 95%)	0.5 % to 1.5 %
Reference(s)	<i>Biomed. Mass. Spectrom.</i> , 1982, 9 , 395-405
Comparability assessment study(ies)	<i>Metrologia</i> , 2003, 40 , <i>Tech. Suppl.</i> , 08003
Comment(s)	The expanded uncertainty is relative
JCTLM DB identification number	NRMeth 80
▸ University of Ghent reference method for glucose	
Applicable matrice(s)	lyophilized, fresh, or frozen human serum
Full description of technique(s)	ID/GC/MS
Quantity	Amount-of-substance concentration
Applicable range	1 mmol/l to 20 mmol/l
Expected uncertainty (level of confidence 95%)	1 % to 2 %
Reference(s)	<i>Clin. Chem.</i> , 1993, 39 , 1001-1006 <i>Clin. Chem.</i> , 1993, 39 , 993-1000 <i>Eur. J. Clin. Chem. Clin. Biochem.</i> , 1996, 34 , 853-860
Comparability assessment study(ies)	EUROMET 563
Comment(s)	The expanded uncertainty is relative
JCTLM DB identification number	NRMeth 4

JCTLM Database: Reference Measurement Service for Glucose

UGent, Belgium	
Phone: +32 (0)9 264 81 04	Contact person: Prof. Dr. L. Thienpont
Fax: +32 (0)9 264 81 98	Email: linda.thienpont@Ugent.be
Analyte	glucose
Material or matrix	blood serum, blood plasma
Quantity	Amount-of-substance concentration
Service measurement range	1 mmol/L to 25 mmol/L
Expanded uncertainty (level of confidence 95%)	1.5 % The expanded uncertainty is calculated for measurement protocol n = 6
Interlaboratory comparison results	RELA - IFCC External Quality assessment scheme for Reference Laboratories in Laboratory Medicine at http://www.dgkl-rfb.de:81/index.shtml
Measurement principle	Isotope dilution gas chromatography mass spectrometry (ID/GC/MS)
JCTLM reference measurement method/procedure	<u>University of Ghent reference method for glucose</u>

Comparison of NMI capabilities for Glucose in Serum Measurements

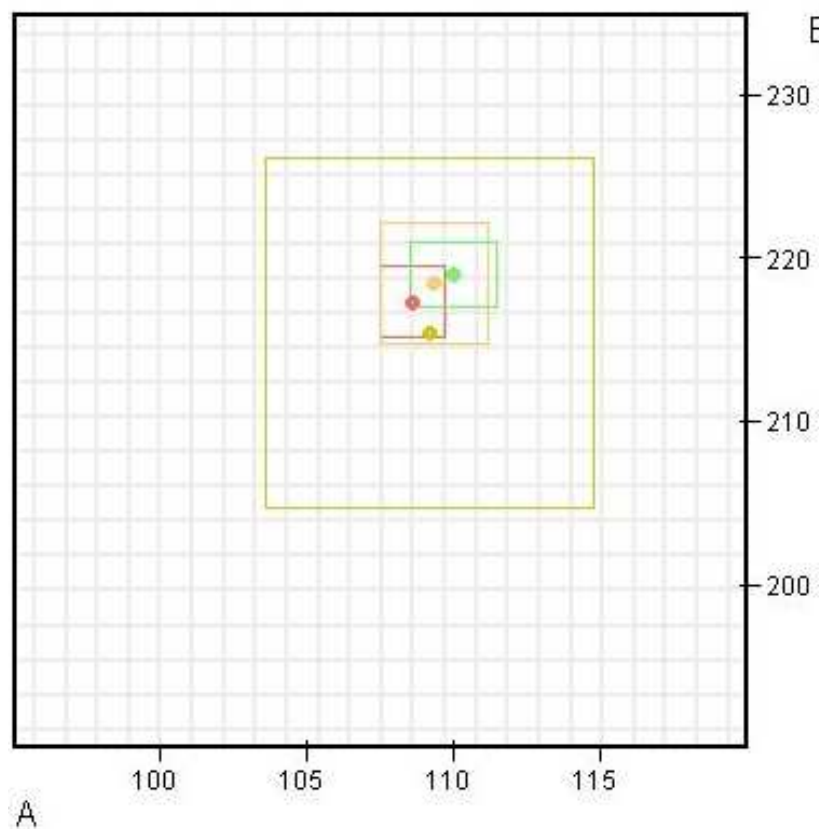
CCQM-K11



IFCC EQUAS results for two different reference methods for glucose in serum

RELA 2004

Glucose [mg/dl]



B

Lab	A	p.e.u.	B	p.e.u.	method
03	108,612	1,081	217,297	2,162	ID-MS
05	109,36	1,86	218,41	3,71	ID-MS
24	109,2	5,59	215,4	10,75	spectrometry
27	110,0	1,45	219,0	1,97	ID-MS

Glucose in Blood, Serum, Urine, CSF
SI-Unit: mmol/l

**Combined
standard
uncertainty (%)**

Section 1 –External to manufacturer, credentialing of the Certified Reference Material

SRM917b

NIST certification of SRM917b (purity)

0.1%

Primary calibrator

SRM917b – weighed amount

Weighing procedure

0.87%

Secondary calibrator

Human Patient Specimens, e.g. Blood, Serum, Urine, CSF

Higher Order Reference Procedure – e.g. Isotope Dilution - Mass Spectrometry or Procedure of Similar Trueness and Precision

Section 2 –Internal to manufacturer, value assignment

Manufacturer's working calibrator

Manufacturer's Master Calibrator, Master Lot of Product Calibrator

Reference Procedure traceable to higher order reference procedure - e.g. Hexokinase/glucose-6-phosphate Dehydrogenase Procedure

1.21%

Product Calibrator

New Lot Commercial Product Calibrator

Procedure applying same chemistry and equipment as routine procedure, but more precisely controlled conditions and more replicates to reduce uncertainty

1.49%

Section 3 –External to manufacturer, End user's results are Traceable to Certified Reference Material and the Reference System

Commercially available system including product reagent and calibrator lots

Routine Sample – Human Patient Specimens, e.g. Blood, Serum, Urine or CSF

RESULT
Glucose in mmol/l

Proficiency Testing Scheme Results for Glucose in Serum

- Results agree with traceable reference value and within acceptance criteria

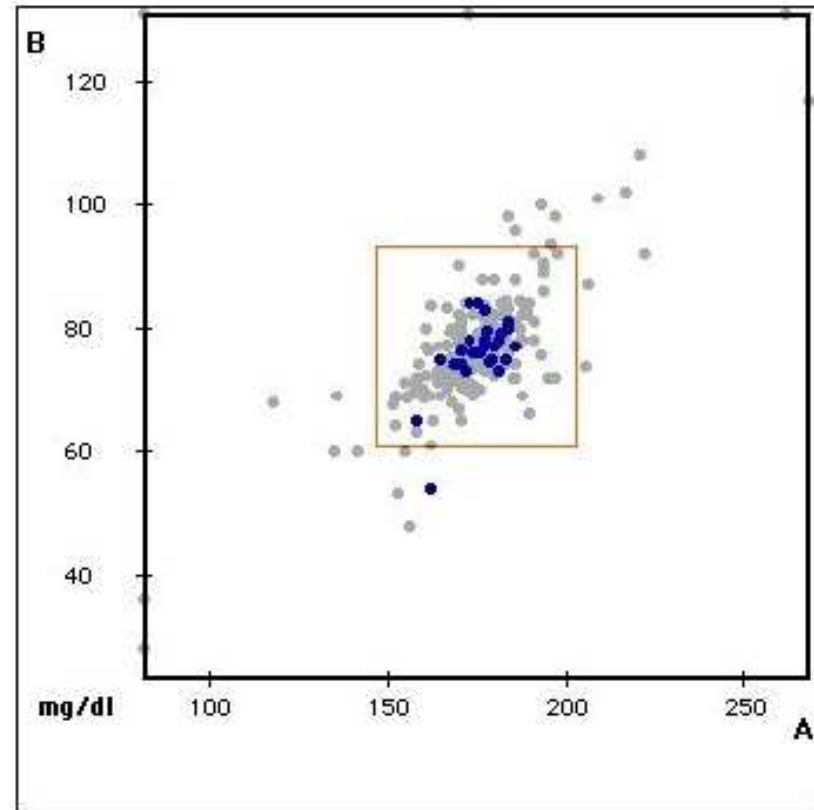
GL4/06

glucose

Hexokinase Reaktion

Split 2

DGKL



selected participants	29	
target value	175	77
limits	147 - 203	60,8 - 93,2
mean value	175,438	75,955
standard deviation	6,536	5,647

Future

JCTLM Activities and Challenges

1. Implementing the revision of ISO 15194
2. Extension of covered List II analytes
3. CRMs with nominal properties
4. Establishing Commutability



Stages of the development of ISO Standards: ISO 15194

- Stage 1: Proposal stage
- Stage 2: Preparatory stage
- Stage 3: Committee stage
- Stage 4: Enquiry stage
- Stage 5: Approval stage
- Stage 6: Publication stage

ISO/DIS 15194

Oct 2007 –ISO/DIS 15194 sent to ISO Central Secretariat

Jan 2008 –FDIS status and final vote by Countries

April 2008 – Approval of new standard

April to Oct 2008 – Publication of new standard in all countries

ISO 15194 Revision

ISO 15194: 2002

In vitro diagnostic medical devices – Measurement of quantities in samples of biological origin – Description of reference materials

ISO/DIS 15194

In vitro diagnostic medical devices – Measurement of quantities in samples of biological origin – Requirements for certified reference materials and the content of supporting documentation

Normative Referenced Documents

4. Systematic format of properties in the supporting documentation of a CRM

ISO 31

6. Content of supporting documentation

6.2 Label

6.3 Certificate

6.4 Certification Report

ISO Guide 31

5. Properties, production and characterization of a CRM

ISO Guide 34

ISO Guide 35

ISO 17511

ISO 18153

GUM

ISO/DIS 15194

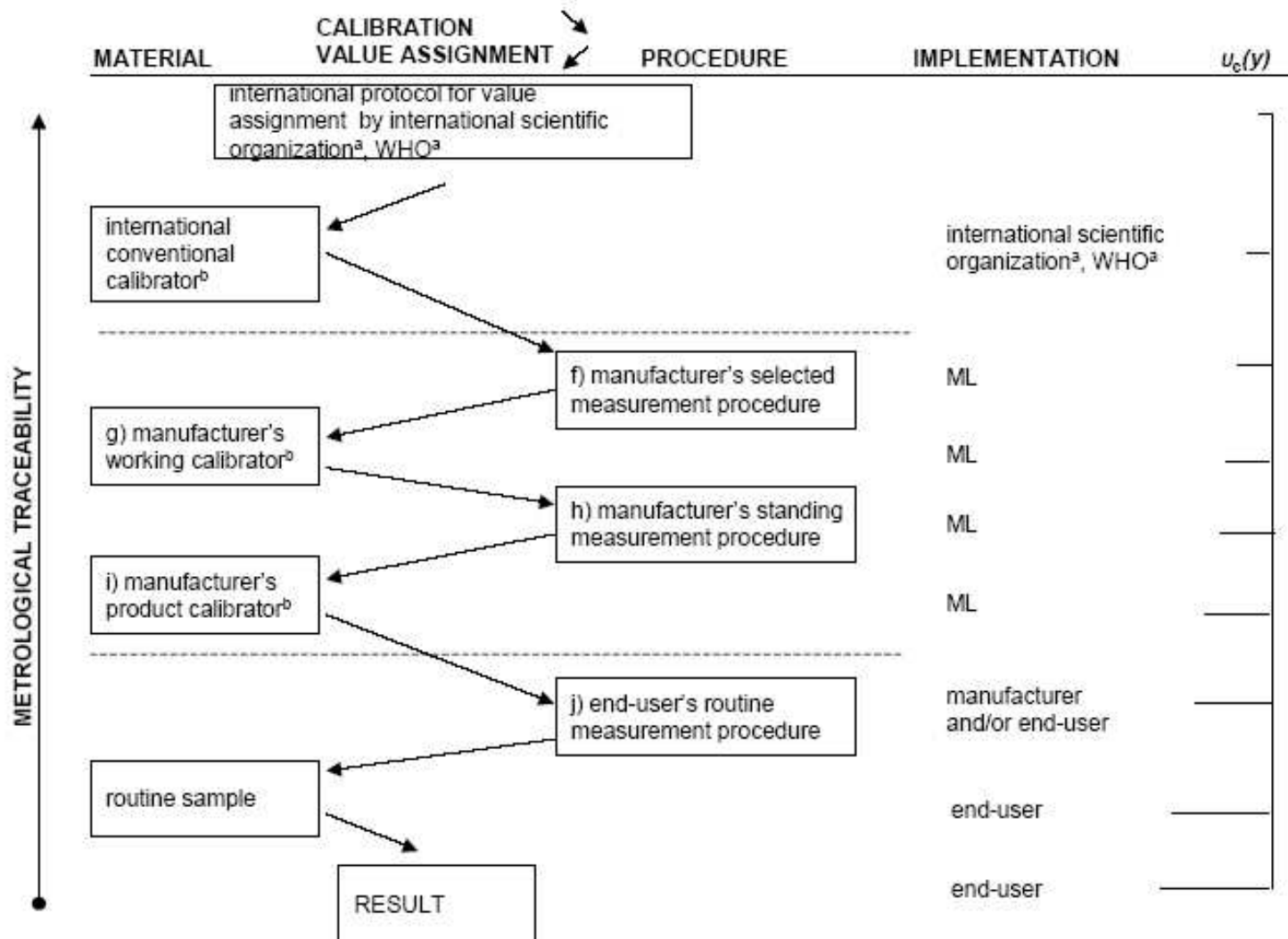
JCTLM LIST II

Reference Materials that are value-assigned using an internationally agreed upon protocol e.g., reference materials for Blood Typing, Coagulation Factors, Microbial Serology, Nucleic Acids, and some Proteins. The values of the measurands in the reference materials on this List are not SI-traceable and/or no internationally-recognized reference measurement procedures exist.

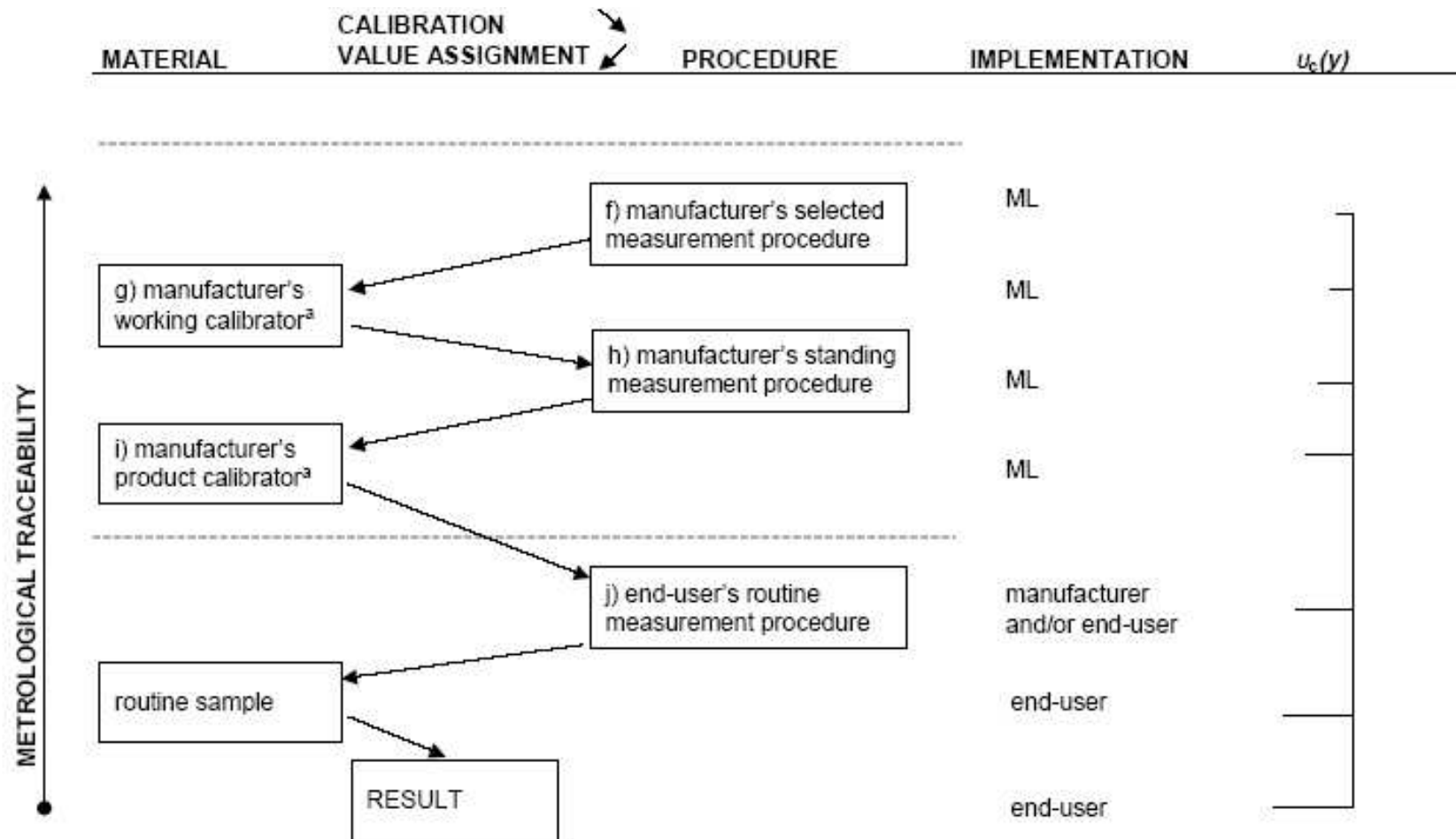
Initially published in January, 2005, now includes

- 21 CRMs for Coagulation Factors
- 7 CRMs for Proteins
- 3 CRMs for Blood Groupings
- 2 CRMs for Enzymes

Traceability to an international conventional calibrator (ISO 17511)



Traceability to manufacturer's selected measurement procedure (ISO 17511)



CRMs with nominal properties or ordinal quantities

- A2. Assigned values cannot be expressed by a numerical value multiplied by a unit of measurement**
- A5. The description of CRMs for nominal properties or ordinal quantities should fulfil, as far as possible, the requirements of CRMs for differential and rational quantities as given in this International standard.**

Exceptions include terminological changes of

- a) quantity to nominal property,**
- b) measurement to examination for nominal properties,**

And technical changes of

- c) using values as those described in A.3 and A.4**
- d) having examination uncertainties expressed as number fractions of misclassification**
- e) not being able to calibrate in relation to a nominal scale**

CRMs with nominal properties or ordinal quantities

The homogeneity and stability of the material shall be demonstrated in view of the relevant properties and quantities

Calibrator Traceability - Commutability

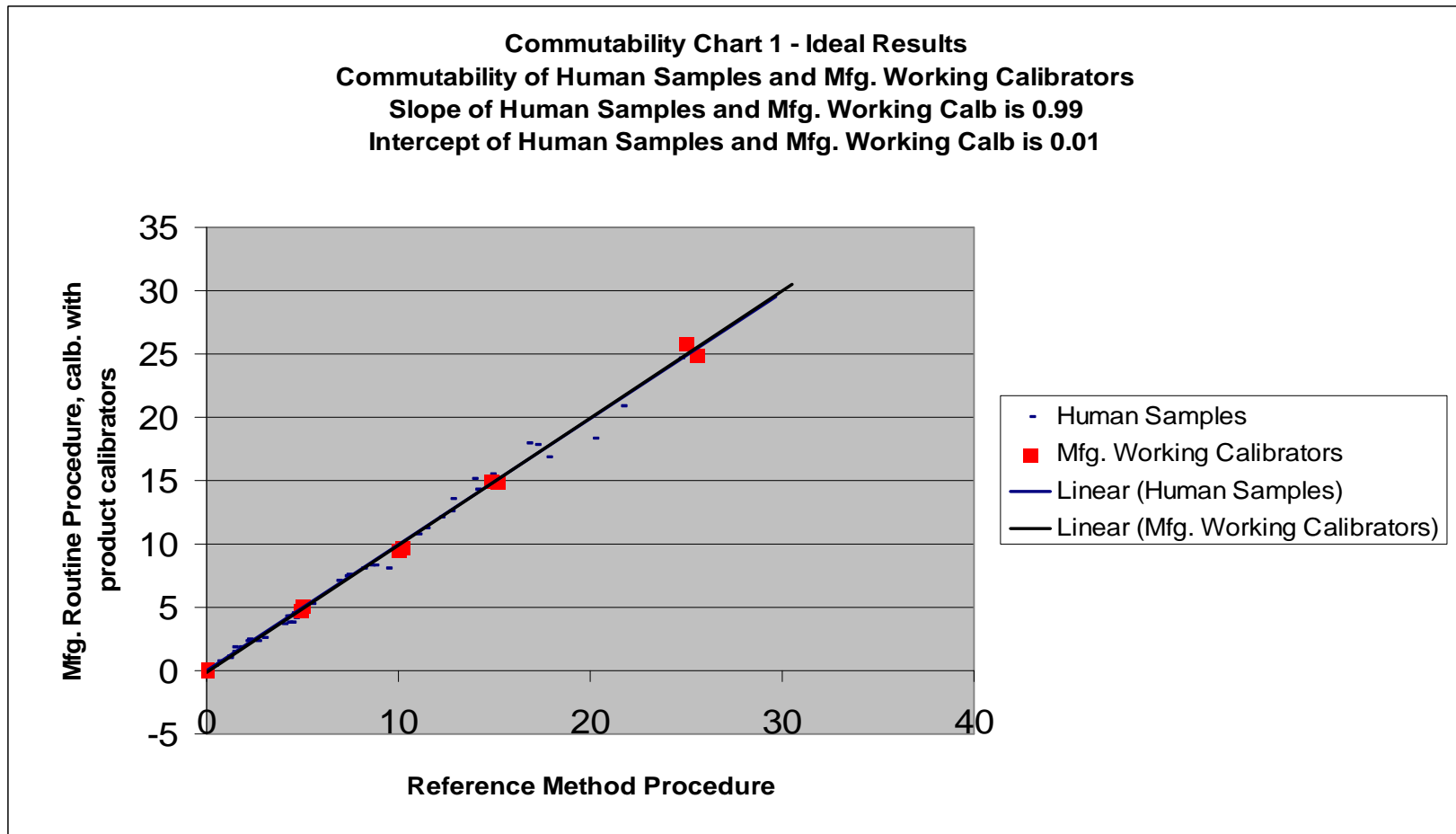
Commutability - Mathematical relationship between the measurement results generated by the measurand in a given calibrator using the reference and the routine procedure is the same as the relationship expected for the measurands in routine human samples.

Commutability of Manufacturer's Working Calibrators assessed by applying the Ref. Meas. Procedure and the Routine Measurement Procedure to the Mfg. Working Calibrator and a set of human samples.

Commutability of Manufacturer's Product Calibrator - compare results of measurements by Ref. Procedure and Routine Procedure on a set of actual samples the the Routine Procedure is intended to be applied.

Results for the Manufacturer's Working Calibrator are consistent with human samples

Calibrator Traceability - Commutability



JCTLM Database : www.bipm.org/jctlm/



Bureau International des Poids et Mesures

Database of higher-order reference materials,
measurement methods/procedures and services



JCTLM Database
Laboratory medicine and *in vitro* diagnostics

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JCTLM database: Laboratory medicine and *in vitro* diagnostics

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↳ Highlights

- ↳ [Extension of the JCTLM-DB](#)
- ↳ [Publication of new data](#)

↳ JCTLM

- ↳ [General information](#)

↳ Analyte keyword search for reference materials, measurement methods/procedures and services

Type an analyte name in part or full, e.g. cholesterol

Refine search by analyte category

Refine search by matrix category

Please select your requirement :

- Higher-order reference materials
- Reference measurement methods/procedures
- Reference measurement services

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